

WE CLAIM:

1. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible polymer; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein said duration of time is from about two weeks to about twelve months after administration.

2. The composition of claim 1, wherein the polymer is a copolymer of lactic acid and glycolic acid.

3. The composition of claim 1, wherein the polymer is a polylactide.

4. The composition of claim 1, wherein the polymer is a caprolactone-based polymer.

5. The composition of claim 1, wherein the polymer is a lactic acid-based polymer.

6. The composition of claim 2, wherein the polymer has L/G ratio of about 50:50 to about 100:0 and a molecular weight ranging from about 3,000 to about 120,000.

7. The composition of claim 1 comprising about 5 wt.% to about 90 wt.% of said biodegradable, biocompatible polymer.

8. The composition of claim 7, comprising about 25 wt.% to about 80 wt.% of said biodegradable, biocompatible polymer.

9. The composition of claim 7, comprising about 35 wt.% to about 75 wt.% of said biodegradable, biocompatible polymer.

10. The composition of claim 1, wherein said duration of time is equal to or greater than three months after administration.

11. The composition of claim 1, wherein said duration of time is from about 3 months to about 6 months after administration.

12. The composition of claim 1, wherein said duration of time is from about 3 months to about 9 months after administration.

13. The composition of claim 1, wherein said duration of time is from about 6 months to about 9 months after administration.

14. The composition of claim 1, wherein the viscous gel further comprises a polymer selected from the group consisting of polylactides, polyglycolides, caprolactone-based polymers, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof, and biodegradable and their copolymers including caprolactone-based polymers, polycaprolactones and copolymers which include polybutylene terephthalate.

15. The composition of claim 1, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

16. The composition of claim 1 wherein the solvent comprises a component solvent selected from the group consisting of triacetin, diacetin, tributyrin,

triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate, triethylglycerides, triethyl phosphate, diethyl phthalate, diethyl tartrate, mineral oil, polybutene, silicone fluid, glycerin, ethylene glycol, polyethylene glycol, octanol, ethyl lactate, propylene glycol, propylene carbonate, ethylene carbonate, butyrolactone, ethylene oxide, propylene oxide, N-methyl-2-pyrrolidone, 2-pyrrolidone, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, caprolactam, decylmethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and mixtures thereof.

17. The composition of claim 1 wherein the solvent is selected from an aromatic alcohol, lower alkyl and aralkyl esters of aryl acids; aryl, aralkyl and lower alkyl ketones; and lower alkyl esters of citric acid.
18. The composition of claim 1 wherein the solvent is benzyl alcohol.
19. The composition of claim 1 wherein the solvent is benzyl benzoate.
20. The composition of claim 1 wherein the solvent is ethyl benzoate.
21. The composition of claim 1, wherein the composition is free of solvents having a miscibility in water that is greater than 7 wt.% at 25°C.
22. The composition of claim 1, wherein said delivery is a systemic delivery.
23. The composition of claim 1, wherein said delivery is a local delivery.
24. The composition of claim 1, wherein said delivery is repeated after a period of time.
25. The composition of claim 1, wherein said delivery is provided at multiple sites.

26. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible polymer; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein the beneficial agent is delivered systemically in a controlled manner over a duration of time is from about two weeks to about twelve months after administration.

27. The composition of claim 26, wherein the polymer is a copolymer of lactic acid and glycolic acid.

28. The composition of claim 26, wherein the polymer is a polylactide.

29. The composition of claim 26, wherein the polymer is a caprolactone-based polymer.

30. The composition of claim 26, wherein the polymer is a lactic acid-based polymer.

31. The composition of claim 27, wherein the polymer has L/G ratio of about 50:50 to about 100:0 and a molecular weight ranging from about 3,000 to about 120,000.

32. The composition of claim 26, comprising about 5 wt.% to about 90 wt.% of said biodegradable, biocompatible polymer.

33. The composition of claim 32, comprising about 25 wt.% to about 80 wt.% of said biodegradable, biocompatible polymer.

34. The composition of claim 32, comprising about 35 wt.% to about 75 wt.% of said biodegradable, biocompatible polymer.

35. The composition of claim 26, wherein said duration of time is equal to or greater than three months after administration.

36. The composition of claim 26, wherein said duration of time is from about 3 months to about 6 months after administration.

37. The composition of claim 26, wherein said duration of time is from about 3 months to about 9 months after administration.

38. The composition of claim 26, wherein said duration of time is from about 6 months to about 9 months after administration.

39. The composition of claim 26, wherein the viscous gel further comprises a polymer selected from the group consisting of polylactides, polyglycolides, caprolactone-based polymers, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof.

40. The composition of claim 26, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

41. The composition of claim 26, wherein the solvent comprises a component solvent selected from the group consisting of triacetin, diacetin, tributyrin, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl

citrate, triethylglycerides, triethyl phosphate, diethyl phthalate, diethyl tartrate, mineral oil, polybutene, silicone fluid, glycerin, ethylene glycol, polyethylene glycol, octanol, ethyl lactate, propylene glycol, propylene carbonate, ethylene carbonate, butyrolactone, ethylene oxide, propylene oxide, N-methyl-2-pyrrolidone, 2-pyrrolidone, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, caprolactam, decylmethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and mixtures thereof.

42. The composition of claim 26, wherein the solvent is selected from an aromatic alcohol, lower alkyl and aralkyl esters of aryl acids; aryl, aralkyl and lower alkyl ketones; and lower alkyl esters of citric acid.

43. The composition of claim 26, wherein the solvent is benzyl alcohol.

44. The composition of claim 26, wherein the solvent is benzyl benzoate.

45. The composition of claim 26, wherein the solvent is ethyl benzoate.

46. The composition of claim 26, wherein the composition is free of solvents having a miscibility in water that is greater than 7 wt.% at 25°C.

47. The composition of claim 26, wherein said delivery is repeated after a period of time.

48. The composition of claim 26, wherein said delivery is provided at multiple sites.

49. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible polymer polymer; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein the beneficial agent is delivered locally in a controlled manner over a duration of time is from about two weeks to about twelve months after administration.

50. The composition of claim 49, wherein the polymer is a copolymer of lactic acid and glycolic acid.

51. The composition of claim 49, wherein the polymer is a polylactide.

52. The composition of claim 49, wherein the polymer is a caprolactone-based polymer.

53. The composition of claim 49, wherein the polymer is a lactic acid-based polymer.

54. The composition of claim 49, wherein the polymer has L/G ratio of about 50:50 to about 100:0 and a molecular weight ranging from about 3,000 to about 120,000.

55. The composition of claim 49, comprising about 5 wt.% to about 90 wt.% of said biodegradable, biocompatible polymer.

56. The composition of claim 55, comprising about 25 wt.% to about 80 wt.% of said biodegradable, biocompatible polymer.

57. The composition of claim 56, comprising about 35 wt.% to about 75 wt.% of said biodegradable, biocompatible polymer.

58. The composition of claim 49, wherein said duration of time is equal to or greater than three months after administration.

59. The composition of claim 49, wherein said duration of time is from about 3 months to about 6 months after administration.

60. The composition of claim 49, wherein said duration of time is from about 3 months to about 9 months after administration.

61. The composition of claim 49, wherein said duration of time is from about 6 months to about 9 months after administration.

62. The composition of claim 49, wherein the viscous gel further comprises a polymer selected from the group consisting of polylactides, polyglycolides, caprolactone-based polymers, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof.

63. The composition of claim 49, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

64. The composition of claim 49, wherein the solvent comprises a component solvent selected from the group consisting of triacetin, diacetin, tributyrin, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate, triethylglycerides, triethyl phosphate, diethyl phthalate, diethyl tartrate, mineral oil, polybutene, silicone fluid, glycerin, ethylene glycol, polyethylene glycol, octanol, ethyl lactate, propylene glycol, propylene carbonate, ethylene carbonate, butyrolactone, ethylene oxide, propylene oxide, N-methyl-2-

pyrrolidone, 2-pyrrolidone, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, caprolactam, decylmethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and mixtures thereof.

65. The composition of claim 49, wherein the solvent is selected from an aromatic alcohol, lower alkyl and aralkyl esters of aryl acids; aryl, aralkyl and lower alkyl ketones; and lower alkyl esters of citric acid.

66. The composition of claim 49, wherein the solvent is benzyl alcohol.


67. The composition of claim 49, wherein the solvent is benzyl benzoate.

68. The composition of claim 49, wherein the solvent is ethyl benzoate.

69. The composition of claim 49, wherein the composition is free of solvents having a miscibility in water that is greater than 7 wt.% at 25°C.

70. The composition of claim 49, wherein said delivery is repeated after a period of time.

71. The composition of claim 49, wherein said delivery is provided at multiple sites.

72. A method of administering a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising: 

(i) administering to a subject :

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible polymer polymer; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel; and

(ii) delivering the beneficial agent to the subject over a duration of time from about two weeks to about twelve months after administration.

73. The method of claim 72, further comprising systemically delivering the beneficial agent to the subject in a controlled manner.

74. The method of claim 72, further comprising repeating the delivering step (ii) after a period of time.

75. The method of claim 73, further comprising repeating the delivering step (ii) after a period of time.

76. The method of claim 72, further comprising locally delivering the beneficial agent to the subject in a controlled manner.

77. The method of claim 76, further comprising repeating the delivery step (ii) after a period of time.

78. The method of claim 76, further comprising conducting the delivery step (ii) at multiple sites.

79. A kit for administration of for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a bioerodible, biocompatible polymer polymer;

(b) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith;

(c) a beneficial agent dissolved or dispersed in the gel; and optionally, one or more of the following:

- (d) an emulsifying agent;
- (e) a pore former;
- (f) a solubility modulator for the beneficial agent, optionally associated with the beneficial agent; and
- (g) an osmotic agent;

wherein at least the beneficial agent, optionally associated with the solubility modulator, is maintained separated from the solvent until the time of administration of the beneficial agent to a subject.

80. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

- (1) a bioerodible, biocompatible blend of polymers; and
- (2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymers and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein said duration of time is from about two weeks to about twelve months after administration.

81. The composition of claim 80, wherein the blend of polymers include a copolymer of lactic acid and glycolic acid.

82. The composition of claim 80, wherein the blend of polymers include a polylactide.

83. The composition of claim 80, wherein the blend of polymers include a caprolactone-based polymer.

84. The composition of claim 80, wherein the blend of polymers include a polymer having an L/G ratio of about 50:50 to about 100:0 and a molecular weight ranging from about 3,000 to about 120,000.

85. The composition of claim 80, comprising about 5 wt.% to about 90 wt.% of said biodegradable, biocompatible polymer.
86. The composition of claim 85, comprising about 25 wt.% to about 80 wt.% of said biodegradable, biocompatible polymer.
87. The composition of claim 85, comprising about 35 wt.% to about 75 wt.% of said biodegradable, biocompatible polymer.
88. The composition of claim 80, wherein said duration of time is equal to or greater than three months after administration.
89. The composition of claim 80, wherein said duration of time is from about 3 months to about 6 months after administration.
90. The composition of claim 80, wherein said duration of time is from about 3 months to about 9 months after administration.
91. The composition of claim 80, wherein said duration of time is from about 6 months to about 9 months after administration.
92. The composition of claim 80, wherein the viscous gel further comprises a polymer selected from the group consisting of polylactides, polyglycolides, caprolactone-based polymers, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof.

93. The composition of claim 80, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

94. The composition of claim 80, wherein the solvent comprises a component solvent selected from the group consisting of triacetin, diacetin, tributyrin, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate, triethylglycerides, triethyl phosphate, diethyl phthalate, diethyl tartrate, mineral oil, polybutene, silicone fluid, glycerin, ethylene glycol, polyethylene glycol, octanol, ethyl lactate, propylene glycol, propylene carbonate, ethylene carbonate, butyrolactone, ethylene oxide, propylene oxide, N-methyl-2-pyrrolidone, 2-pyrrolidone, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, caprolactam, decylmethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and mixtures thereof.

95. The composition of claim 80, wherein the solvent is selected from an aromatic alcohol, lower alkyl and aralkyl esters of aryl acids; aryl, aralkyl and lower alkyl ketones; and lower alkyl esters of citric acid.

96. The composition of claim 80, wherein the solvent is benzyl alcohol.

97. The composition of claim 80, wherein the solvent is benzyl benzoate.

98. The composition of claim 80, wherein the solvent is ethyl benzoate.

99. The composition of claim 80, wherein the composition is free of solvents having a miscibility in water that is greater than 7 wt.% at 25°C.

100. The composition of claim 80, wherein said delivery is a systemic delivery.

101. The composition of claim 80, wherein said delivery is a local delivery.

102. The composition of claim 80, wherein said delivery is repeated after a period of time.

103. The composition of claim 80, wherein said delivery is provided at multiple sites.

104. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible blend of polymers; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymers and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein the beneficial agent is delivered systemically in a controlled manner over a duration of time is from about two weeks to about twelve months after administration.

105. An injectable depot composition for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible blend of polymers; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymers and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel;

wherein the beneficial agent is delivered locally in a controlled manner over a duration of time is from about two weeks to about twelve months after administration.

106. A method of administering a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

(ii) administering to a subject :

(a) a viscous gel formulation comprising:

(1) a bioerodible, biocompatible blend of polymers; and

(2) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymers and form a gel therewith; and

(b) a beneficial agent dissolved or dispersed in the gel; and

(ii) delivering the beneficial agent to the subject over a duration of time from about two weeks to about twelve months after administration.

107. The method of claim 106, further comprising systemically delivering the beneficial agent to the subject in a controlled manner.

108. The method of claim 106, further comprising repeating the delivering step (ii) after a period of time.

109. The method of claim 107, further comprising repeating the delivering step (ii) after a period of time.

110. The method of claim 106, further comprising locally delivering the beneficial agent to the subject in a controlled manner.

111. The method of claim 110, further comprising repeating the delivery step (ii) after a period of time.

112. The method of claim 110, further comprising conducting the delivery step (ii) at multiple sites.

113. A kit for administration of for sustained delivery of a beneficial agent to a subject in a controlled manner over a predetermined duration of time after administration comprising:

- (a) a bioerodible, biocompatible blend of polymers;
- (b) a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymers and form a gel therewith;
- (c) a beneficial agent dissolved or dispersed in the gel; and optionally, one or more of the following:
- (d) an emulsifying agent;
- (e) a pore former;
- (f) a solubility modulator for the beneficial agent, optionally associated with the beneficial agent; and
- (g) an osmotic agent;

wherein at least the beneficial agent, optionally associated with the solubility modulator, is maintained separated from the solvent until the time of administration of the beneficial agent to a subject.